



Rasayana Chikitsa as Adjuvant Therapy in Cancer Survivorship: Mechanism and Evidence Review

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ABSTRACT

Cancer survivors increasingly experience treatment-related morbidity - fatigue, myelosuppression, neuropathy, and impaired quality of life (QoL) - that persists well beyond active oncological treatment. Rasayana Chikitsa, the Ayurvedic discipline of rejuvenation and Vyadhikshamatva (host-resistance) enhancement, has been explored as a complementary adjuvant strategy to mitigate these sequelae. This review synthesises classical conceptual foundations of Rasayana with contemporary mechanistic and clinical evidence, focusing on immunomodulation, antioxidant and anti-inflammatory pathways, and chemo-/radio-protective effects of key Rasayana dravyas such as Ashwagandha (*Withania somnifera*), Guduchi (*Tinospora cordifolia*), and compound formulations including Brahma Rasayana and Rasayana Avaleha. While preclinical data robustly support multi-targeted modulation of NF- κ B, STAT3, and PI3K/AKT signalling along with antioxidant and immune-enhancing activity, clinical evidence remains limited to small trials, observational cohorts, and case reports. Rasayana therapy appears to offer a biologically plausible, low-toxicity adjunct for improving QoL and reducing treatment-related toxicity in cancer survivorship, but rigorous randomised controlled trials are needed before definitive clinical recommendations can be made.

I. Introduction

Cancer survivorship is now recognised as a distinct and increasingly important phase of oncological care, extending from the completion of primary treatment through long-term follow-up and encompassing the prevention and management of treatment-related complications, surveillance for recurrence, rehabilitation, and optimisation of quality of life [1]. Survivors frequently experience persistent physical, psychological, cognitive, and immunological sequelae collectively referred to as the "late effects" of cancer and its treatment. Fatigue, chronic pain, chemotherapy-induced peripheral neuropathy, cognitive dysfunction, anxiety, depression, sleep disturbances, sexual dysfunction, metabolic

derangements, and immune dysregulation often persist long after successful completion of therapy, substantially affecting functional status and overall well-being [2-4]. The growing recognition of these challenges has shifted the focus of cancer care from merely prolonging survival to improving survivorship outcomes and restoring long-term health.

Globally, the burden of cancer continues to rise. According to the Global Cancer Observatory (GLOBOCAN) 2022 estimates, approximately 20 million new cancer cases and 9.7 million cancer-related deaths occurred worldwide, while nearly 53.5 million individuals were living within five years of a cancer diagnosis [5-6].

Demographic ageing, population growth, and lifestyle transitions are expected to increase this burden substantially over the coming decades. Simultaneously, advances in screening, precision diagnostics, surgery, radiotherapy, chemotherapy, targeted therapy, and immunotherapy have significantly improved survival rates across many malignancies, resulting in an expanding population of cancer survivors with unique long-term healthcare needs [7].

Despite these therapeutic advances, conventional anticancer treatments frequently produce cumulative toxicities that persist beyond treatment completion. Chemotherapy and radiotherapy may induce chronic inflammation, oxidative stress, mitochondrial dysfunction, immune impairment, endocrine abnormalities, and accelerated biological ageing. These alterations contribute to fatigue, frailty, organ dysfunction, reduced physical performance, and diminished health-related quality of life [8-10]. Current survivorship guidelines therefore increasingly advocate comprehensive supportive care strategies encompassing symptom management, rehabilitation, nutritional optimisation, psychological support, exercise, and evidence-based complementary interventions to improve long-term outcomes [11-12].

Within this context, integrative oncology has emerged as a patient-centred discipline that combines evidence-informed complementary therapies with standard cancer treatment to improve symptom control, functional recovery, and quality of life without compromising oncological efficacy. Rather than replacing conventional treatment, integrative oncology seeks to safely complement surgery, chemotherapy, radiotherapy, immunotherapy, and targeted therapy by addressing the multidimensional needs of cancer survivors through personalised supportive care [13].

Ayurveda offers one such complementary framework through *Rasayana Chikitsa*, one of the eight classical clinical specialities (*Aṣṭāṅga Ayurveda*). *Rasayana* is fundamentally directed toward promoting longevity (*Dīrghāyū*), preserving physiological function, enhancing tissue quality (*Dhātu-Sārātā*), optimising metabolic homeostasis through balanced *Agni*, maintaining proper *Srotas* function, strengthening *Vyādhiḥṣamatva* (host defence), and nourishing *Ojas*, the classical determinant of vitality and resilience. Classical Ayurvedic texts describe *Rasayana* therapy as improving physical strength, cognitive function, immunity, complexion, and resistance to disease, while slowing age-related degeneration. These holistic objectives closely parallel several modern survivorship goals, including restoration of physiological reserve, mitigation of treatment-related toxicity, enhancement of immune competence, reduction of chronic inflammation, and improvement of overall quality of life [14-16].

Contemporary experimental research has begun to provide mechanistic support for these traditional concepts. Several

Rasayana medicinal plants-including *Withania somnifera* (*Ashwagandha*), *Tinospora cordifolia* (*Guduchi*), *Phyllanthus emblica* (*Amalaki*), *Glycyrrhiza glabra* (*Yashtimadhu*), and polyherbal Rasayana formulations-have demonstrated antioxidant, anti-inflammatory, immunomodulatory, adaptogenic, anti-fatigue, radioprotective, chemoprotective, and tissue-reparative properties in preclinical investigations [17-19]. Proposed mechanisms include modulation of oxidative stress pathways, regulation of NF-κB, Nrf2, STAT3, and PI3K/Akt signalling, attenuation of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, enhancement of endogenous antioxidant enzymes, preservation of mitochondrial function, and support of innate and adaptive immune responses. Although these findings are promising, the available clinical evidence remains heterogeneous, with relatively few well-designed randomised controlled trials specifically evaluating Rasayana interventions in cancer survivorship [20-22].

Accordingly, there is an increasing need for a comprehensive synthesis that critically integrates classical Ayurvedic concepts with contemporary biomedical evidence. Such an appraisal may help identify plausible biological mechanisms, evaluate current clinical evidence, recognise methodological limitations, and define priorities for future translational research [23-26].

The present review therefore examines the theoretical foundations, proposed molecular mechanisms, preclinical evidence, and available clinical studies regarding *Rasayana Chikitsa* as an adjuvant therapy in cancer survivorship. By integrating classical Ayurvedic principles with contemporary oncological science, this review aims to provide clinicians and researchers with an evidence-based overview of the potential role of Rasayana therapy in improving survivorship outcomes while highlighting areas requiring further high-quality clinical investigation [27-30].

2. Classical Conceptual Framework of *Rasayana* in Relation to Neoplastic Disease

- Classical Ayurvedic literature does not describe cancer as a distinct disease entity analogous to the modern concept of malignancy. Instead, pathological conditions characterised by abnormal tissue growth and persistent swellings are described under entities such as *Arbuda* and *Granthi*. Among these, *Arbuda*, described in *Sushruta Samhita*, is considered the closest conceptual correlate of neoplastic disease because of its deep-seated origin, progressive enlargement, relative immobility, chronic course, and poor prognosis, whereas *Granthi* denotes relatively smaller and well-circumscribed swellings [31].
- The pathogenesis (*Samprapti*) of *Arbuda* is explained through *Dosha-Dushya Sammurchana*, wherein aggravated *Doshas*-predominantly *Kapha* and *Vata*-interact with susceptible *Dhatus*, particularly *Mamsa*,

Meda, and *Rakta*. Impaired *Agni* and *Srotorodha* further disturb tissue metabolism and nutrition, fundamentally from the molecular basis of carcinogenesis, they reflect a systemic understanding of chronic tissue pathology rather than an isolated local lesion [32].

- Within this conceptual framework, *Rasayana Chikitsa* is regarded as a restorative therapeutic approach that supports normal tissue homeostasis and enhances the body's adaptive capacity following chronic disease. Consequently, in contemporary integrative oncology, *Rasayana* is being investigated as an adjuvant strategy to complement standard cancer therapy by supporting recovery and long-term survivorship rather than acting as a primary antineoplastic treatment [33].

3. Proposed Molecular Mechanisms

3.1 Antioxidant and Anti-inflammatory Activity

A substantial body of preclinical evidence indicates that classical *Rasayana* dravyas exert antioxidant effects through upregulation of endogenous antioxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase) and scavenging of reactive oxygen species (ROS) generated by chemotherapy and ionising radiation. Several *Rasayana* botanicals also modulate pro-inflammatory signalling, prominently nuclear factor-kappa B (NF-κB), a master regulator of inflammatory cytokine expression that is frequently constitutively activated in malignant cells and implicated in chemoresistance. Inhibition of NF-κB activation has been demonstrated for Withaferin A, a principal withanolide of *Ashwagandha*, contributing to reduced inflammation-driven tumour-promoting signalling [34].

3.2 Pro-apoptotic and Antiproliferative Signalling

Multiple *Rasayana*-derived phytoconstituents demonstrate induction of apoptosis in malignant cell lines through

resulting in abnormal tissue proliferation and progressive disease. Although these concepts differ interaction with key signalling nodes including NF-κB, STAT3, PI3K/AKT, and the Bcl-2/Bax axis. Withaferin A has been shown to induce reactive-oxygen-species-mediated apoptosis selectively in breast cancer cell lines (MCF-7, MDA-MB-231) while sparing normal mammary epithelial cells, with additional reported activity against Hsp90 stabilisation, survivin signalling, and G2/M cell cycle arrest [35].

3.3 Antiangiogenic Effects

Inhibition of vascular endothelial growth factor (VEGF)-mediated angiogenesis has been documented for Withaferin A in experimental tumour models, suggesting a mechanism by which *Rasayana* constituents may limit the vascular supply necessary for tumour growth and metastatic spread [36].

3.4 Immunomodulation

Guduchi (*Tinospora cordifolia*) and *Ashwagandha* have both demonstrated enhancement of natural killer (NK) cell activity and macrophage function in experimental models, supporting the classical *Rasayana* claim of strengthened *Vyadhikshamatva*. This immune-enhancing activity is particularly relevant in the context of chemotherapy-induced myelosuppression and immune compromise during survivorship [37].

3.5 Chemo- and Radio-protective Effects

Beyond direct antineoplastic mechanisms, several *Rasayana* formulations appear to function primarily as cytoprotective adjuvants - mitigating normal-tissue toxicity from chemotherapy and radiotherapy. *Brahma Rasayana* has been shown in preclinical studies to restore radiation-depleted hepatic antioxidant enzymes and accelerate haematopoietic recovery, while reducing markers of metastatic spread [38].

Table 1. Representative *Rasayana* dravyas and their mechanistic correlates in oncology [39-45]

Rasayana Dravya	Classical Attribution	Principal Mechanistic Targets	Reported Clinical/Preclinical Effect
Ashwagandha (<i>Withania somnifera</i>)	Charaka Samhita, Chikitsa Sthana	NF-κB, STAT3, PI3K/AKT inhibition; ROS-mediated apoptosis; VEGF-mediated antiangiogenesis	Reduced chemotherapy-induced fatigue and toxicity; radiosensitization in preclinical models
<i>Guduchi</i> (<i>Tinospora cordifolia</i>)	Charaka, Sushruta Samhita	Immunomodulation (NK cell, macrophage activation); antioxidant enzyme upregulation	Myeloprotective and hepatoprotective support during chemoradiotherapy
<i>Brahma Rasayana</i>	Charaka Samhita, Chikitsa Sthana 1	Antioxidant enzyme restoration; hematopoietic recovery	Reduced metastatic spread and radiation-induced antioxidant depletion in preclinical

			studies
Rasayana Avaleha (compound formulation)	Contemporary compound Rasayana formulation	Multi-targeted cytoprotection against chemoradiotherapy toxicity	Controlled clinical trial showed reduced adverse effects vs. chemoradiotherapy alone

4. Clinical and Translational Evidence

4.1 Controlled and Observational Studies

A controlled clinical evaluation of Rasayana Avaleha administered alongside chemoradiotherapy in cancer patients reported reduced treatment-related adverse effects compared with chemoradiotherapy alone, supporting the cytoprotective rationale described above. Observational studies of herbomineral Rasayana therapy have similarly reported improvements in quality-of-life metrics among patients with advanced cancer [46-50].

4.2 Case Reports and Case Series

A growing body of case literature describes individualised Rasayana Therapy (ART) protocols used either as adjuvant support alongside conventional treatment or, in selected chemo-intolerant patients, as an alternative approach [51-54]. Reported outcomes include disease-free survival of several years in early-stage breast cancer following Rasayana therapy after surgery in a patient who declined adjuvant chemotherapy, and a documented case of tumour regression in chemo-intolerant stage IV follicular lymphoma managed with Ayurvedic Rasayana Therapy [55-57]. A separate case report described complete tumour regression using an exclusive Rasayana regimen in high-grade diffuse large B-cell lymphoma. These reports, while methodologically limited to single-patient observations, are noteworthy for documenting imaging-confirmed outcomes and standardised performance-status assessment (ECOG) [58-60].

4.3 Synthesis Across the Evidence Base

Recent narrative reviews converge on a consistent picture: preclinical evidence for multi-targeted anticancer and cytoprotective activity of Rasayana botanicals is extensive and mechanistically coherent, whereas clinical evidence remains largely confined to small trials, observational cohorts, and case reports rather than adequately powered randomised controlled trials [61-62]. A 2025 review specifically addressing Rasayana therapy in cancer prevention and survivorship concluded that clinical use shows particular promise in improving quality of life, reducing cancer-related fatigue, and mitigating chemotherapy-induced toxicities such as myelosuppression and neuropathy, with additional potential for chemosensitising and radioprotective effects [63-66].

5. Discussion

The convergence between the classical Ayurvedic

construct of Vyadhikshamatva and the modern survivorship-care goals of immune restoration, toxicity mitigation, and quality-of-life improvement provides a coherent rationale for integrating Rasayana Chikitsa into supportive oncology. Mechanistically, the multi-targeted activity of Rasayana phytoconstituents - spanning antioxidant, anti-inflammatory, pro-apoptotic, antiangiogenic, and immunomodulatory pathways - contrasts with the single-target specificity of most conventional oncological agents, and may explain reported synergy with chemoradiotherapy in reducing normal-tissue toxicity.

However, several limitations constrain translation into clinical guidelines. Most clinical data derive from small, often single-centre studies or individual case reports without randomisation or blinding, limiting causal inference. Standardisation of herbal formulations, variability in withanolide and other active-constituent content across sources, and limited pharmacokinetic and bioavailability data further complicate dose-response interpretation [67-68]. Drug-herb interaction potential, particularly with concurrent chemotherapeutic agents, also requires systematic evaluation, as multi-targeted immunomodulation could theoretically interfere with certain mechanisms of cytotoxic or immunotherapeutic agents.

Future research priorities include adequately powered randomised controlled trials with standardised Rasayana formulations, validated patient-reported outcome measures (e.g., EORTC QLQ-C30) alongside classical Ayurvedic assessment parameters, pharmacovigilance studies addressing herb-drug interactions, and mechanistic studies correlating Dosha-Prakriti-based patient stratification with biomarker response - an approach consistent with the personalised-medicine direction of contemporary oncology [69].

6. Conclusion

Rasayana Chikitsa offers a biologically plausible and classically well-grounded adjuvant strategy for cancer survivorship care, supported by robust preclinical evidence of multi-targeted antioxidant, anti-inflammatory, pro-apoptotic, antiangiogenic, and immunomodulatory activity. Early clinical signals suggest benefit in reducing chemoradiotherapy-related toxicity and improving quality of life, but the evidence base remains predominantly preclinical and observational. Larger, methodologically rigorous clinical trials are needed before Rasayana therapy can be recommended as a standard component of

integrative survivorship care, though its low-toxicity profile and mechanistic coherence justify continued

structured clinical investigation.

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